• **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Cefpiramide RS

Cefpiramide for Injection

DEFINITION
Cefpiramide for Injection contains NLT 90.0% and NMT 120.0% of the labeled amount of cefpiramide ($C_{25}H_{24}N_8O_7S_2$).

IDENTIFICATION
• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

Change to read:

• **PROCEDURE**
Buffer: 1.36 g/L of monobasic potassium phosphate in water adjusted with 1 N sodium hydroxide to a pH of 6.8 ± 0.1 before final dilution
Mobile phase: Tetrahydrofuran, acetonitrile, methanol, and *Buffer* ■(40:40:40:880)■1S *(USP35)*
System suitability solution: 1 mg/mL of USP Cefpiramide RS in 0.01 N sodium hydroxide. Heat this solution at 95° for 10 min. Dilute 1 mL of this solution with *Mobile phase* to 20 mL. This solution contains a mixture of cefpiramide and cefpiramide lactone.
Standard solution: 0.25 mg/mL of USP Cefpiramide RS in *Mobile phase*
Sample solution 1 (where it is represented as being in a single-dose container): Constitute a container of Cefpiramide for Injection in a volume of water corresponding to the volume of diluent specified in the labeling. Withdraw all of the withdrawable contents, using a suitable hypodermic needle and syringe, and dilute with *Mobile phase* to obtain a solution containing the nominal equivalent of 0.25 mg/mL of cefpiramide.
Sample solution 2 (where the label states the quantity of cefpiramide in a given volume of constituted solution): Constitute a container of Cefpiramide for Injection in a volume of water equivalent to the volume of diluent specified in the labeling. Dilute the constituted solution with water to obtain a solution nominally containing 0.25 mg/mL of cefpiramide.
Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: LC
Detector: UV 254 nm
Column: ■4.0-mm × 15- to 30-cm; 5- to 10-µm packing L7■1S *(USP35)*
Flow rate: 1.5 mL/min
Injection size: 20 µL
System suitability
Samples: *System suitability solution* and *Standard solution*
[NOTE—The relative retention times for cefpiramide and cefpiramide lactone are 0.7 and 1.0, respectively.]
Suitability requirements
Resolution: NLT 5 between cefpiramide lactone and cefpiramide, *System suitability solution* ■■1S *(USP35)*
Tailing factor: 0.95–1.4, *Standard solution*
Relative standard deviation: NMT 2.0%, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution 1* or *Sample solution 2*

Calculate the percentage of cefpiramide ($C_{25}H_{24}N_8O_7S_2$) withdrawn from the container, or in the portion of constituted solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of the *Sample solution*
r_S = peak response of the *Standard solution*
C_S = concentration of USP Cefpiramide RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of cefpiramide in *Sample solution 1* or *Sample solution 2* (mg/mL)
Acceptance criteria: 90.0%–120.0%

SPECIFIC TESTS
• **PYROGEN TEST** ⟨**151**⟩
Sample solution: 50 mg/mL of cefpiramide from Cefpiramide for Injection in Sterile Water for Injection
Test dose: 1.0 mL/kg of the *Sample solution*
Acceptance criteria: Meets the requirements
• **STERILITY TESTS** ⟨**71**⟩**:** It meets the requirements when tested as directed for *Test for Sterility of the Product to Be Examined, Membrane Filtration*.
• **pH** ⟨**791**⟩
Sample solution: Equivalent to 100 mg/mL of cefpiramide from Cefpiramide for Injection
Acceptance criteria: 6.0–8.0 in water
• **WATER DETERMINATION,** *Method I* ⟨**921**⟩**:** NMT 3.0%
• **PARTICULATE MATTER IN INJECTIONS** ⟨**788**⟩**:** It meets the requirements for small-volume injections.

ADDITIONAL REQUIREMENTS
• **PACKAGING AND STORAGE:** Preserve as described in *Injections* ⟨1⟩*, Containers for Sterile Solids*.
• **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Cefpiramide RS

Add the following:

■Celecoxib

$C_{17}H_{14}F_3N_3O_2S$ 381.4
4-[5-(4-Methylphenyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl] benzenesulfonamide;
p-[5-*p*-Tolyl-3-(trifluoromethyl)pyrazol-1-yl] benzenesulfonamide [169590-42-5].

DEFINITION
Celecoxib contains NLT 98.0% and NMT 102.0% of $C_{17}H_{14}F_3N_3O_2S$, calculated on the anhydrous basis.

IDENTIFICATION
• **A. INFRARED ABSORPTION** ⟨**197**⟩**:** [NOTE—Methods ⟨197A⟩, ⟨197K⟩, or ⟨197M⟩ under *Infrared Absorption* may be used.]
[NOTE—If the spectra obtained show differences, dissolve the substance to be examined and the Reference Standard separately in isopropyl alcohol, evaporate to dryness, and record the new spectra.]
• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY
• **PROCEDURE**
Buffer: 2.7 g/L of monobasic potassium phosphate adjusted with phosphoric acid to a pH of 3.0 ± 0.2

Mobile phase: Methanol, acetonitrile, and *Buffer* (3:1:6)
Diluent: Methanol and water (3:1)
System suitability solution: 0.5 mg/mL of USP Celecoxib RS and 2.4 µg/mL each of USP Celecoxib Related Compound A RS and USP Celecoxib Related Compound B RS in *Diluent*
Standard solution: 0.5 mg/mL of USP Celecoxib RS in *Diluent*
Sample solution: 0.5 mg/mL of Celecoxib in *Diluent*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 215 nm
Column: 4.6-mm × 25-cm; 5-µm packing L11
Column temperature: 60°
Flow rate: 1.5 mL/min
Injection size: 25 µL
Run time: About 1.5 times the celecoxib peak elution
System suitability
Samples: *System suitability solution* and *Standard solution*
Suitability requirements
Resolution: NLT 1.8 between celecoxib related compound A and celecoxib and NLT 1.8 between celecoxib and celecoxib related compound B, *System suitability solution*
Relative standard deviation: NMT 0.73%, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of $C_{17}H_{14}F_3N_3O_2S$ in the portion of Celecoxib taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of the *Standard solution* (mg/mL)
C_U = concentration of the *Sample solution* (mg/mL)
Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

Inorganic Impurities

• **HEAVY METALS:** NMT 20 ppm
Diluent: Acetone and water (17:3)
Standard solution: Dilute 1.0 mL of *Standard Lead Solution*, prepared as directed under *Heavy Metals* ⟨231⟩, *Special Reagents*, with *Diluent* to 20 mL.
Sample solution: Dissolve 0.50 g of Celecoxib in 20 mL of *Diluent*.
Blank solution: 20 mL of *Diluent*
Analysis
Samples: *Standard solution*, *Blank solution*, and *Sample solution*
To each solution, add 2 mL of *pH 3.5 Acetate Buffer*, prepared as directed under *Heavy Metals* ⟨231⟩, *Method I*. Mix, and add to each solution 1.2 mL of thioacetamide–glycerin base TS. Mix immediately, and allow to stand for 2 min. Pass the solutions through a filter of 0.45-µm pore size. Compare the spots on the filters obtained from each of the solutions.
Acceptance criteria: The brownish-black color of the spot resulting from the *Sample solution* is not more intense than that of the spot resulting from the *Standard solution*. The test is invalid if the *Standard solution* does not show a brownish-black color compared to the *Blank solution*.

• **RESIDUE ON IGNITION** ⟨**281**⟩**:** NMT 0.2%, using a platinum crucible

Organic Impurities

• **PROCEDURE**
Buffer, Mobile phase, Diluent, System suitability solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.
Standard solution: 0.5 µg/mL of USP Celecoxib RS in *Diluent*
System suitability
Samples: *System suitability solution* and *Standard solution*
Suitability requirements
Resolution: NLT 1.8 between celecoxib related compound A and celecoxib and NLT 1.8 between celecoxib and celecoxib related compound B, *System suitability solution*
Signal-to-noise ratio: NLT 20, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of each impurity in the portion of Celecoxib taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response for each impurity in the *Sample solution*
r_S = peak response of celecoxib in the *Standard solution*
C_S = concentration of celecoxib in the *Standard solution* (mg/mL)
C_U = concentration of Celecoxib in the *Sample solution* (mg/mL)
Acceptance criteria
Individual impurities: See *Table 1*.
[NOTE—Disregard any impurity peak less than 0.05%.]

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Celecoxib related compound A[a]	0.9	0.4
Celecoxib	1.0	—
Celecoxib related compound B[b]	1.1	0.10
Individual unspecified impurity	—	0.10
Total impurities	—	0.5

[a] 4-[5-(3-Methylphenyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl] benzenesulfonamide.
[b] 4-[3-(4-Methylphenyl)-5-(trifluoromethyl)-1*H*-pyrazol-1-yl] benzenesulfonamide.

SPECIFIC TESTS

• **WATER DETERMINATION,** *Method I* ⟨**921**⟩**:** NMT 0.5%, using a 400-mg sample

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in tight containers, protected from light and moisture. Store at room temperature.
• **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Celecoxib RS
p-[5-*p*-Tolyl-3-(trifluoromethyl)pyrazol-1-yl] benzenesulfonamide.
$C_{17}H_{14}F_3N_3O_2S$ 381.4
USP Celecoxib Related Compound A RS
4-[5-(3-Methylphenyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl]benzenesulfonamide.
$C_{17}H_{14}F_3N_3O_2S$ 381.4
USP Celecoxib Related Compound B RS
4-[3-(4-Methylphenyl)-5-(trifluoromethyl)-1*H*-pyrazol-1-yl]benzenesulfonamide.
$C_{17}H_{14}F_3N_3O_2S$ 381.4 ■1S (*USP35*)